

benzoic acid, 5.9 cc. of 1N. sodium hydroxide and 1 g. of p-fluorophenacyl chloride in 20 cc. of 95 per cent alcohol was refluxed for 1 hour and the reaction product obtained on cooling or by precipitation with small amounts of water. The esters may be readily recrystallized from 95 per cent alcohol.

p-Fluorophenacyl-o-nitrobenzoate crystallizes in very slightly yellow microscopic needles, melting at 74.5°C. to a clear oil.

*Anal.* Calcd. for  $C_{15}H_{10}O_5NF$ : nitrogen, 4.6. Found, 4.5.

p-Fluorophenacyl-m-nitrobenzoate separates in colorless glistening needles, melting at 105°C. to a clear colorless oil.

*Anal.* Calcd. for  $C_{15}H_{10}O_5NF$ : nitrogen, 4.6. Found, 4.5.

p-Fluorophenacyl-p-nitrobenzoate crystallizes in slightly yellow needles, melting at 134°C. to a clear oil.

*Anal.* Calcd. for  $C_{15}H_{10}O_5NF$ : nitrogen, 4.6. Found, 4.7.

#### SUMMARY

p-Fluorophenacyl alcohol and several of its esters have been prepared and described.

PHARMACOLOGY.—*The nitrite-thiosulphate combination as a remedy for cyanide poisoning in sheep.*<sup>1</sup> H. BUNYEA, J. F. COUCH, and A. B. CLAWSON, Bureau of Animal Industry.

In a former paper<sup>2</sup> the results of experiments with remedies for cyanide poisoning in sheep and cattle were reported. It was found that, of the remedies tried, a combination of sodium nitrite and sodium thiosulphate<sup>3</sup> was the most effective for cattle. The combination was not used on sheep at that time, but the results of the cattle experiments left little doubt that it would also prove to be the most effective remedy in the case of poisoned sheep.

The experimental methods used were the same as those already reported<sup>2</sup> and do not need extended repetition here. The cyanide was administered *per os* as potassium cyanide solution, freshly prepared, and the remedies were injected intraperitoneally, using 10 per cent solutions for the smaller doses and 20 per cent for the larger.

The results are given in Table I. Twenty-two experiments were performed with 18 animals of which 13 died. The doses were varied beginning with 2 m.l.d. calculated according to the figure previously reported for the m.l.d. (2.315 mg. per kg.), and rising gradually to 3.5 m.l.d. Table 2 is an analysis of these data and shows the effectiveness of the remedy against the various doses.

<sup>1</sup> Received November 1, 1934.

<sup>2</sup> This JOURNAL 24: 369-395. 1934.

<sup>3</sup> This remedy was first suggested by E. Hug., C.r.Soc. Biol. 114: 711-714. 1933.

TABLE 1.—NITRITE-THIOSULPHATE AS A REMEDY FOR CYANIDE POISONING IN SHEEP

Date	Sheep	Weight	Dose	Time from drench—			Remedy		Effect
				to first symptoms	to collapse	to giving remedy	Sodium nitrite	Sodium thiosulphate	
1934	No.	kg.	m.l.d.	min.	min.	min.	g.	g.	
May 8	1111	49.9	2	1	2.5	5.5	1	1	Survived
9	1113	50.8	2.25	1	1.5	2.5	1	2	Survived
8	1244	43.5	2.5		1.5	3	1	2	Died
9	1111	49.9	2.5	0.5	2	4	1	3	Survived
8	1113	50.8	2.5		1	2	1	2	Survived
15	1111	49.9	2.75	0.5	1.5	2.5	1	3	Survived
15	1113	50.8	2.75	1	1.5	2	1	3	Survived
23	1465	29.9	2.75	1	1.25	6	1	3	Died
23	1456	29.5	2.75	1	1	5.5	1	3	Died
23	1459	35.8	2.75	0.75	1.5	15	1	3	Survived
8	11730	38.1	3	1	1.5	3	1	2	Died
8	1241	34.5	3	1	1	2.5	1	2	Died
Aug. 30	1507	36.2	3	1	2	2	3	2	Died
30	102A	32.6	3	1	1.5	1.5	1	2	Died
30	1578	40.35	3	1.25	1.25	1.5	1	4	Died
31	1556	37.2	3	1	1.5	1.5	2	2	Survived
Sept. 11	1561	42.6	3	1.5	4	4.5	2	3	Died
11	1560	37.2	3	1	1.5	2	2	3	Died
11	1572	35.8	3.5	1.5	2	2	2	3	Survived
11	1487	39	3.5	1.5	2	2	2	3	Died
11	1479	41.2	3.5	0.5	1.5	1.5	2	4	Died
11	1499	39.9	3.5	1	2	2	2	4	Died

It is plain that, if administered promptly, the remedy is reasonably effective against 2.75 m.l.d. of cyanide in sheep as against 2 m.l.d. in cattle. Of 5 sheep that received this large dose, three survived and two died. In the latter cases the remedy was withheld until the animals were in the gasping stage and thus the test of the remedy was very severe. One of the sheep that survived, No. 1459 was not given the remedy until 15 minutes after the completion of the drench. This animal was unusually resistant to the cyanide and after exhibiting early symptoms began to improve instead of becoming progressively worse. This condition persisted for some 12 minutes during which

TABLE 2.—EFFECTIVENESS OF THE REMEDY AGAINST VARYING DOSES OF CYANIDE

Dose m.l.d.	Number of animals	Survived	Died	Per cent survival
3.5	4	1	3	25
3	8	1	7	12.5
2.75	5	3	2	60
2.5	3	2	1	66
2.25	1	1	0	100
2	1	1	0	100

time the sheep rose to his feet and remained standing a few seconds. He then began to stagger, went down on the belly and exhibited the usual train of symptoms shown by the other cases. Administration of the remedy was now withheld until the sheep appeared to be in a condition similar to that of the other sheep 3 to 4 minutes after drenching.

In our work on cyanide poisoning we have occasionally found resistant animals that show irregular behavior during the course of the sickness. Two other cases of similar behavior were encountered recently which will be reported in another paper of this series. Aside from these cases the course of the sickness with the poisoned animals was similar to that already described.

#### THE EFFECT OF AN INCREASED DOSE OF SODIUM NITRITE

Since little was known about the proper dose of sodium nitrite for sheep the question arose whether a dose larger than 1 gram might not be more effective. Nitrites are themselves quite toxic and there would be a dosage above which the remedy might itself cause or contribute to the death of the animal.

TABLE 3.—TOXICITY OF SODIUM NITRITE INJECTED INTRAPERITONEALLY

Date 1934	Sheep No.	Weight kg.	Dose mg./kg.	Actual dose g.	Effect
Aug. 31	1471	31.7	47.3	1.5	Died
" 31	1479	41.2	48.8	2	Survived
" 30	1521	34.45	58	2	Died
" 31	1516	42.6	70.4 <sup>a</sup>	3	Survived
" 31	1482	31.7	78.8	2.5	Died
" 31	1480	34.9	84.8	3	Survived
" 31	1490	41.7	95.9 <sup>a</sup>	4	Died
" 30	1527	34.4	113.3	4	Died
" 30	1504	38.09	120.7	4	Died
" 30	1499	39.9	150.3	6	Survived
Sept. 5	1499	39.9	150.3	6	Survived
Aug. 30	1467	40.8	195.9	8	Died

<sup>a</sup> Plus 2g. of sodium thiosulphate.

As a preliminary measure several sheep were given varying doses of sodium nitrite intraperitoneally. The data are detailed in Table 3. It is apparent that the effect of sodium nitrite is quite variable since four of the animals poisoned survived doses larger than proved fatal with other sheep and one, No. 1499, on two occasions survived the second largest dose given although 6 sheep were killed by much

smaller doses and one died on one-third as much. Owing to the variability it was impossible to draw conclusions about the m.l.d. The symptoms exhibited by the sheep consisted of depression and accelerated respiration. In sheep No. 1521 the rate of respiration reached 148 per minute within 10 minutes after injecting the nitrite and in sheep No. 1504, 152 per minute. Two experiments were made to obtain evidence as to whether the simultaneous injection of sodium thiosulphate would influence the toxicity of sodium nitrite. In neither case was there any apparent antagonism between the two salts.

The experiments led to the conclusion that a one gram dose of sodium nitrite intraperitoneally is the safest for remedial use and two grams is the largest dose that should be administered and then only under exceptional circumstances.

There remained the possibility that in actual cyanide poisoning the toxic effect of the nitrite might be counteracted by the cyanide and warrant the use of larger doses of sodium nitrite. To test this possibility eight sheep were given 3 m.l.d. of potassium cyanide and 4 were given 3.5 m.l.d. by mouth and immediately upon collapsing were treated with varying doses of sodium nitrite combined with sodium thiosulphate. The results are summarized in Table 4.

TABLE 4.—EFFECT OF INCREASED DOSES OF SODIUM NITRITE

Dose m.l.d.	NaNO <sub>2</sub> g.	Na <sub>2</sub> S <sub>2</sub> O <sub>4</sub> g.	Number of animals	Survived	Died
3	1	2	3		3
3	1	4	1		1
3	2	2	1	1	
3	2	3	2		2
3	3	2	1		1
3.5	2	3	2	1	1
3.5	2	4	2		2

From these figures it is apparent that increasing the dose of sodium nitrite did not alter the final outcome of the poisoning.

#### SUMMARY

The combination of sodium nitrite and sodium thiosulphate protects with reasonable certainty against 2.75 m.l.d. of cyanide particularly when the remedy is administered promptly.

Increasing the dose of nitrite to 2 and 3 g. did not result in improvement while introducing an unfavorable element due to the toxicity of the nitrite itself.

Increasing the dose of thiosulphate may have resulted in some



improvement and does not, of itself, introduce another toxicity factor.

The nitrite-thiosulphate combination was definitely more effective with sheep than with cattle.

Doses of sodium nitrite above 95 mg. per kg. are likely to be fatal and above 50 mg. per kg. are dangerous. The safest therapeutic dose that can be recommended for cyanide poisoning is 1 g. intraperitoneally for a 75 to 90 pound (35 to 40 kg.) sheep and 2 g. is the largest dose that should be given.

PALEONTOLOGY.—*Celliforma spirifer, the fossil larval chambers of mining bees.*<sup>1</sup> ROLAND W. BROWN, U. S. Geological Survey.  
(Communicated by JOHN B. REESIDE, JR.)

The 1930 Smithsonian expedition, led by C. W. Gilmore to the Bridger Basin in southwestern Wyoming, brought back to the National Museum among its collection of fossils a handful of curious, solid objects (Fig. 3) that have remained unidentified. These specimens were found by George B. Pierce in surface material weathered from the lower strata of the fresh-water Bridger formation of upper Eocene age, about 6 miles southeast of Mountainview, Wyo., in sec. 18, T. 14 N., R. 14 W.

The natural size sketch (Fig. 3) illustrates several of the more perfect specimens. They average 2.7 centimeters in length by 1.2 centimeters in diameter. They are greenish gray to white in color, smooth, and round; but many are slightly flattened and bent like a bean; most show the effects of former breakage and partial collapse and now superficially resemble cracked but not disintegrated eggshells. The apex is a low dextral spiral of four or five turns making an inconspicuously scalloped and pitted groove. In some examples the apex is an almost flat spiral, in others the last turns form a narrow prominent blunt point.

Numerous sections disclosed no internal cellular structure or organic remains of any kind. The matrix of the unbroken specimens is calcite; that of the more or less broken specimens is calcite and greenish clay. It is clear that the calcite crystallized in a cavity, sometimes filling the cavity completely, sometimes leaving empty pockets to be filled or not with clay.

Speculation about these objects ranged from snake eggs to date seeds, on which latter probability they were referred to me for identification. A search of the literature and the seed collections, however,

<sup>1</sup> Published by permission of the Director, U. S. Geological Survey. Received October 30, 1934.